Readers Summary

1. Why I use highly sensitive C-reactive protein (CRP) and Vitamin D as biomarker proxies.
2. After Leptin, Cortisol is the next most important domino to fall.
3. Hormone Cascade explained in a paragraph.
4. Unintended consequences of hypercortisolism destroy health.
5. Initial HS-CRP signals the genesis of underlying hormonal disruption (First sign Leptin is toast).

Now that we have laid some foundation about Leptin at the “30-foot research level” (I know, I made your head hurt at times), let’s zoom out now and look at how this affects the hormones that dictate the things patients see and feel and sense about their bodies.

I want to now give you some perspective as to WHY this matters

We have established that as one gets fat, Leptin levels rise. Once they get high enough (around a Body Mass Index (BMI) of 20-24), Tumor Necrosis Factor (TNF) rises in several tissues. This also causes a rise of NF kappa beta and IL-6 in the brain. TNF quickly destroys normal hepatic homeostasis, which sets the stage for fatty liver disease and type two diabetes over time. This rise in TNF also biochemically changes Leptin receptor signaling and changes its quantum properties by changing its “resonance” (think of a vibration-like effect in the receptor) at the hypothalamus level. Once TNF rises, it
causes the liver to make an acute phase inflammatory protein called highly sensitive CRP. HS-CRP is therefore a very early biomarker for cellular inflammation before any disease is established. We have already established in earlier blogs that inflammation causes Leptin resistance. Leptin controls all energy production in the body. Inflammation stops T4 to T3 conversion in the liver and abruptly turns off your thyroid’s ability to function properly despite normal thyroid labs. As an analogy, your car engine no longer has a gas pedal to use. Simultaneously Vitamin D production caves as well because TNF takes that out too. Immunity fails and bad things commence for the cellular terroir.

In summary, once Leptin resistance occurs centrally in the brain, the liver soon follows and then the peripheral tissues become resistant, too. This affects fecundity, bone metabolism, cardiac metabolism, the thyroid, and the immune system in that order. Are you with me?

**Resultant Hormone Cascade**

Leptin resistance occurs first. Then *insulin resistance* happens next. This eventually leads to adrenal resistance. Cortisol is the stress hormone that allows for fight or flight syndrome (life or death). This is the hormone that allows you to run away from a hungry lion fast and live. Evolution always makes sure cortisol production stays ready for action at the expense of the other hormones that also are made from the same precursors. That precursor is pregnenolone. Pregnenolone is made from cholesterol, and cholesterol is made from LDL. So anytime the body is stressed or inflamed, it up-regulates cholesterol production to make more lifesaving hormones. It requires T3 and vitamin A as cofactors to complete this step. Blocking cholesterol production will increase cellular stress. This is why biochemically, to me, no statin drugs have ever made any sense under any circumstance in medicine. Moreover, this is why there is a chronic association of cancer to low
cholesterol levels in the literature. If your cholesterol levels are low, you can not properly construct a mitotic spindle to pull apart your chromosomes correctly. This is why cancer rates have been shown to be higher in 11 studies on statins. This has been documented in the literature and the Great Cholesterol Con, by Anthony Colpo. In times of infection or stress, LDL levels always need to rise to protect the cell to make more cholesterol to make hormones and improve intracellular signaling.

A diet should provide a substrate of animal protein to sustain the hormone substrates. This is why a Paleo diet is ideal for hormone health because it provides ample substrate for all hormones. A Paleolithic diet is best for longevity in my opinion. It supports all of our hormones that are present in abundance in youth and health. Many other physicians, like Dr. Ron Rosedale, tell folks that protein stimulates the mTOR pathway which leads to death. The real issue I have here is that he gives no context to the statement. Here is my context. His belief is only true if the background cellular terroir has a high HS CRP backdrop, and if your gut is leaky as shown by a low HDL level and high EMF exposure. If your HS CRP is treated aggressively with an Epi-Paleo high fat seafood diet, your HS CRP will be low and your HDL will be high, and then a moderate protein diet is protective. If Ron was right then the recent data on primate longevity would have supported his beliefs, but they have not to date. The reason was simple. The data Dr. Rosedale used to form this belief was generated in 1930. The Environmental EMF risks of 1930 no longer exist so the results of those experiments hold no validity to us today. Today’s modern world has different variables that dramatically affect DNA and RNA expression.

So I go hard after HS CRP in all of the patients I work with. It is a staple in my practice. Once solved, it is hard-core ancestral template advice to affect the performance aspects of life. The most important part of our biology is wellness and
disease reversals, and this is when the Epi-Paleo Rx should be your go-to move. Leptin Resistance trumps cortisol in the human cascade in the brain and body. Cortisol is a slow acting hormone.

**Hormones.** So anytime cellular stress is high (high HS CRP), it also forces all the hormone backbone substrate called pregnenolone to be shunted to cortisol production. This is called pregnenolone steal syndrome. What exactly does this mean, Doc? DHEA, Androstenedione, Vitamin D, testosterone, estrogen, and aldosterone production all fall dramatically. These are all of the hormones that are made from a common precursor. Remember that chronic Leptin resistance leads to huge hypercortisolism all the time! Never forget this Biological Fact! So that means we need to understand well what high cortisol does to the cellular terroir as well (Levee 1).

This also means that Leptin resistance clinically will lead to low vitamin D levels. This completely explains the epidemic that John Cannell, MD is reporting about in the Vitamin D council newsletters. This, in turn, down-regulates T regulator cells of the immune system, and it will decrease bone metabolism as well since vitamin D is a cofactor in bone metabolism. Since DHEA and Androstenedione are lowered, too, the sex steroids are also lowered because they are made from DHEA and Andro. In younger humans, this leads to early andropause, low libido, and early onset perimenopause anytime stress is present. When this occurs in older humans, like postmenopausal women, it destroys libido and electrolyte balance (low aldosterone effects) and causes osteopenia and osteoporosis. Younger females lose control of fecundity, oocyte maturation, and get amenorrhea. Evolution does not favor these activities when your stress hormone is high. It favors survival over these other activities. This observation was mind shattering to my practice when I realized it. In men, longevity is tied to their optimized testosterone levels.

The high cortisol also directly affects the Hypothalamic-
pituitary-adrenal (HPA) axis. Cortisol directly blocks 5′ deiodinase enzyme that converts T4 to T3 (this occurs in the liver). Cortisol Releasing Hormone (CRH) (seen elevated in high cortisol production states) directly blocks TSH. The implication is huge because Thyroid Stimulating Hormone (TSH) and T3, the active thyroid hormone, are inhibited quickly in this process. Immediately, any excess T4 is then shunted to reverse T3. Reverse T3 is a COMPETITIVE inhibitor to T3, the active thyroid hormone. This basically turns off the thyroid! (You’re welcome ladies.), This is a biological switch needed to shut metabolism off in starvation mode. This is precisely what happens in starvation or in anorexia. Once T3 is turned off, no fat burning can occur at the muscles with UCP3. Remember, UCP3 activation requires T4, T3, and Leptin to be working well. With high cortisol, it cannot. Shutting off these things could be good biologically if you’re badly starving or if you’re morbidly obese. CRH also directly inhibits TSH. This is why TSH is a horrible marker for thyroid status. If you do not know the cortisol status, you can infer zero information from a thyroid panel. This is reason number one for many thyroid misdiagnoses. The sad part is that most endocrinologists seem to have forgotten this vital biochemical fact. It is the source of most patient frustrations with their thyroid condition.

CRH directly blocks secretion of Growth Hormone secretion as well. This means you get sarcopenia and osteopenia together! Low GH levels (IGF1) increase your body fat, decrease your lean muscle mass and increase your osteopenia to a great degree. It also causes the cardiac muscle to fail and decreases the stroke volume. Sarcopenia is the result of low IGF1 or GH level, and is a harbinger of ensuing death, especially with respect to the heart. There is now excellent data to support the use of GH and testosterone for cardiac health in aging because of these effects. High cortisol comes from stress. The causes of stress in humans are: psychological, traumatic, infectious, allergic,
electromagnetic (EMF), xenobiotic and geopathic, as well as Leptin resistance and dysbiosis.

**Key points about cortisol**

1. Anything that causes a chronic elevation of cortisol causes chronic disease.
2. Any chronic elevation of cortisol and insulin will lead to some kind of chronic disease and death.
3. Signs and symptoms that you really have stress and a cortisol problem will cause most mainstream medicine docs to put you on one or more of these ten medications:
   - Statin
   - Premarin
   - Synthroid
   - Prilosec
   - Hydrocodone
   - Norvasc
   - Glucophage / Metformin
   - Albuterol
   - Claritin
   - Prozac/sleeping pills.

The reason is simple. There is no good blood test available for serum cortisol that is accurate, and western doctors do not realize the salivary cortisol tests are deadly accurate. NASA and the FAA use salivary testing for their screening of astronauts and pilots. When I see this combo of drugs, I know from the demographic page on a patient’s medical chart that we likely have an undiagnosed cortisol problem without any test. I generally will eventually prove my clinical suspicion with a salivary cortisol assay. So they listen to the symptoms of the patients and treat the symptoms, and not the underlying cause, HYPERCORTISOLISM. By far, the number one cause in the USA is Standard American Diet loaded with too many carbs or too much PUFA’s, which drives Leptin resistance and adiposity. Both raise TNF alpha. We are now back at the top of the post. The
circle of life in one post. You now are an endocrinologist. Actually, you may now know more than they do.

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